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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,588	12/03/2004	Eishun Tsuchida	0020-5327PUS1	9917
2292 7590 07/05/2007 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			EXAMINER AUDET, MAURY A	
			ART UNIT 1654	PAPER NUMBER
			NOTIFICATION DATE 07/05/2007	DELIVERY MODE ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/516,588	<b>Applicant(s)</b> TSUCHIDA ET AL.	
	<b>Examiner</b> Maury Audet	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 01 June 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,3,5 and 7-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3,5 and 7-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 December 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### DETAILED ACTION

Applicant's amendment and response of 3/6/07 is acknowledged. Amended claims 1, 3, 5, and 7-15 are examined on the merits.

#### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of claims 1, 3, 5, and 7-15 under 35 U.S.C. 103(a) as being obvious over Tsuchida et al. I (Bioconjugate Chem., 1999, 10, 797-802), and Tsuchida et al. II (Bioconjugate Chem., 2000, 11, 46-50). [Applicant's earlier publications], is maintained for the reasons of record.

The claims have been examined as a product – namely, an oxygen infusion ‘composition’, though the latter has not (yet) been inserted, or the like to clarify product; unless the alternative is sought (method). Claim 1 is to “An oxygen infusion [composition] for increasing an oxygen concentration in tumor tissues in living bodies . . .”. Upon close review of Applicant's response to the outstanding rejection, the arguments are substantively directed to “effects/outcomes”, which may bear weight as to “methods of use” subject matter but not as to products as presently claimed/examined. The intended use (e.g. method) of the products does not impute patentable weight into a known or obvious product. The arguments speak to a new

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method of using the known porphyrin metal complexes (in cancer cells, as opposed to normal cells, as originally intended). Four examples follow:

1. Page 13-14 "Tsuchida II fails to teach or suggest the *effects* of the porphyrin metal complex-clathrate albumin compound on the oxygen partial pressure in tumor tissues".
2. Page 14, 1<sup>st</sup> full para, line 2, Applicant argues that "Thus, *the behaviors of porphyrin metal complexes in normal cells differ from that of porphyrin metal complexes in cancer cells*".
3. Page 11, last para, line 1, Applicant's asserts that "the invention makes it possible to effectively increase the oxygen partial pressure in tumor tissues".
4. Similarly, on page 14, 3<sup>rd</sup> full para., line 2, Applicant's traverses that "Such an effect of the present invention is never expected from the cited references [Applicant's own previous works]..."

Thus, the substance of the rejection is maintained and repeated below for continuity of record.

Tsuchida et al. I teach that substituted amido phenylporphinatoiron(II)s (FePs) are incorporated in hydrophobic cavities of recombinant human serum albumin (rHSA), providing a synthetic O<sub>2</sub> carrier hemoprotein under physiological conditions. ( col.3, line 65). However, Tsuchida et.al. I does not teach the finding of cyclic amido phenylporphynatoiron (II).

Tsuchida et al. II teach that amidophenylporphinatoiron (II) analogs which are structurally very similar to the present substituted porphyrins in combination with albumin show a good activity in the anesthetized rats (page 47, results and discussion).

It would be been obvious to one of ordinary skill in the art at the time of the invention to make the substituted cyclic 1-methyl cyclohexanyl amido phenylporphinatoiron (II) in

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Tsuchida et al. I, because Tsuchida et al. II advantageously teach minor structural changes between this compound and the compounds made by Tsuchida I which would have been merely routine structural optimization by one of ordinary skill in the art to apply the substitutions of represented by the porphyrin of Tsuchida II; **because it binds oxygen better**. One of ordinary skill in the art would have readily ascertained that this would be an the result (rather than being unexpected).

Tsuchida et. al. I also showed that human serum albumin (HSA) incorporating synthetic hemes (FeP)s is an artificial hemoprotein (HSA-FeP) which is able to reversibly bind and release dioxygen under physiological conditions. The physiological response to exchange transfusion with HSA and (FeP)s into the rats was also taught. The reference also determined the half-life of deoxygenated HSA-FeP.

It would be been obvious to one of ordinary skill in the art at the time of the invention to modify the compound of Formula I wherein R contains a methyl cyclohexanol substitution in Tsuchida et al. I because Tsuchida et al. I advantageously teach a nearly identical compound and one of ordinary skill in the art would have been motivated to make this substitution in Tsuchida et al. I alone (or in view of Tsuchida et al. II) in order to modify the phenylporphinatoiron (II) and use albumin clatherate as a dispersion.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at

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the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

***Claim Observation***

If Applicant is in fact claiming a product (as examined), it is suggested that "composition" be inserted after the term "infusion". If a method of use is being claimed, Applicant may wish to consider the filing of a continuation application to so pursue.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.


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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 6/23/2007



CHRISTOPHER R. TATE  
PRIMARY EXAMINER